Yale University

Department of Psychology
P.O. Box 11A Yale Station
New Haven, Connecticut 06520-7447

Campus address:
2 Hillhouse Avenue.

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Angela Potter
Administrative Grants Officer
ONR--Resident Representative
495 Summer Street, Room 103
Boston, MA 02210-2109

Re: Final Technical Report on ONR grant 00014-90-4136

Dear Ms. Potter:

Following is the final technical report on the grant "Self-Organization of Hebbian Synapses on Hippocampal Neurons" (N00014-90-4136), a copy of which has also been sent to Dr. Thomas McKenna as well as to Defense Technical Information Center (DITC).

To reverse-engineer the learning machinery of the brain it is necessary to determine the computations performed by biological neurons and neural circuits and to implement these on a fast platform. This requires defining the device characteristics of the individual neurons and the mechanisms of use-dependent synaptic plasticity.

Our hypothesis has been that learning is a function not only of the training data set but also of the properties of the individual neurons—especially their electrotonic architecture, active membrane properties, and synaptic modification (learning) mechanisms. We have made great strides in unearthing basic neuronal mechanisms and speeding up implementations of neuronal models. This last effort was done in collaboration with computer scientists and a local company that specializes in circuit simulations using fast parallel implementations.

The research has produced numerous publications and abstracts plus presentations at several meetings. There have been major technical, theoretical, and experimental break-throughs. The new technology will result in commercial developments and significant scientific advances. Transitions to industry have been numerous.

The near-term objective of this original proposal was to create models of the key types of hippocampal neurons and be able to implement these on a sufficiently fast platform that we could extract some of their key features. This effort involved a collaboration with Dr. Brenda Claiborne, who was principally responsible for the anatomical aspects of this project.

- As promised, we developed computational models of all of the principal types of hippocampal neurons—CA3 pyramidal neurons, CA1 pyramidal neurons, and granule cells of the dentate gyrus. Several papers on these model neurons have been published already [1, 2] [3-15] and several more have been submitted or are about to be submitted. A master's thesis was completed on this and is being readied for publication along with three Ph.D dissertations. Together, these will

result in 8 - 10 additional publications. In addition, one of my new students is creating models of the inhibitory interneurons, which we know to be critical at the circuit level, which is our current interest (see below).

● Also as promised, we also succeeded in accelerating the implementation of these models, via parallel software that runs on parallel supercomputers or workstation clusters. This is been done using LINDA. In concert with this effort, the Yale Advanced Technology Center, which I founded, hired several relevant scientists to work on aspects of this work. One was Michael Hines, who had made very impressive advances on the development of NEURON, which you probably know now runs on PCs. From my previous progress reports, you realize that we have had significant interactions with and technology transfers to industry.

Much of the initial work centered on the effects of the passive cable properties. but more recent efforts have begun to incorporate various types of nonlinear dynamics and to examine how these interact with various types of synaptic learning rules [16, 17]. There are numerous practical implications for this initial work, which we are continuing under current ONR support. The goal of building silicone brains that learn is no longer far-fetched. Since the ultimate purpose of much work on intelligent systems is to create learning systems, this has been my focus.

● In ONR grant 00014-90-4136, the creation and simulation of model neurons gave me an intimate intuition about how neurons compute. Under the present ONR grant, I have been building on these intuitions to create a completely novel mechanism for associative spatio-temporal learning. Actually, it is not completely novel, as this may be the mechanism that the brain actually uses.

● The transition has been a gradual one—from trying to understand self-organizing systems (the topic of the ONR grant that has just ended) to using this information but also including the objective of accounting for goal-directed or supervised learning. At the synaptic level, of course, we have a good idea that something like a Hebbian mechanism is probably involved [16, 18-27] and this is not hard to implement. The real challenge is to understand how this comes together at the circuit-level. In particular, we need to know how space and time encoded using neuron-like elements.

Until recently, I have been doing these simulations in my head, and they have been working. I now have students collecting the key data and running the circuit simulations to verify my intuitions in this regard, but I am rarely wrong in these matters—that is, usually the simulations simply specify the exact numerical values of the parameters necessary to achieve the intuited result. In the past we have delivered on some key relevant discoveries—demonstrating the existence of Hebbian synapses, showing how they self-organize as a function of their input and electrotonic structure, and devising a whole new theoretical approach to cable theory.

● Now I believe we can bring all of this plus non-linear membrane dynamics into the circuit level in a way that is not hard to implement and can capture key aspects of supervised spatio-temporal learning in a novel and fascinating manner. I am hoping to have the first simulation of this done within the next year along with the experimental data demonstrating that the postulated mechanisms actually exist in just the right places. Educating myself further in

animal learning theory and interactions with the laboratories of Nelson Donnegon and Alan Wagner have been very useful in imposing a top town structure on this collection of devices and microcircuits that we have come to understand.

● Regarding other matters, a final financial report was previsously sent under separate cover by our Office of Grants and Contracts. Similarly, they have or will soon send the signed Report of Inventions and Subcontracts form (#882) and the Augmentation Awards form (#A2-2). In regard to the latter, the supported graduate student, Anders Greenwood, has completed his Ph. D work and will do his final dissertation defense on September 26, 1995. He has lined up a Postdoctoal Fellowship at U.C San Francisco Medical School, which will entail working with Robert Malenka and Roger Nicoll, both top neuroscientists.

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Sincerely,

Thomas H Br

Thomas H. Brown, Ph. D
Professor of Psychology and Cellular and Molecular Physiology